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EXAMINER	
TUNG, JOYCE	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
03/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,689	ALLAIRE, NORMAND E.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/31/07,5/15/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed 8/31/07 has been entered. Claims 19-59 are pending.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 37 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 37 is vague and indefinite because it is unclear what the abbreviation "MGB" stands for. Clarification is required.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 19-27, 34-35 and 39-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Romano et al. (6,093,542, issued Jul. 25, 2000).

Romano et al. disclose an isothermal transcription based amplification assay for the detection and quantitation of MDC RNA (See column 2, lines 30-32). The assay has all the components as recited in the claims. The method starts with an RNA template in which a double stranded DNA is generated by a reverse transcription and then the double stranded DNA is used as template for large amount of RNA synthesis by a RNA polymerase (See column 2, lines 42-

48). One of the primers has, in addition to the sequences complementary to the template, an additional sequences necessary for generating an RNA promoter (See column 2, lines 49-52). The single stranded RNA product is detected by hybridization with a labeled oligonucleotide (See column 2, lines 53-56 and column 5, lines 56-59). The samples come from various body tissues or cells (See column 2, lines 61-63). The sample may be total RNA extracts (See column 5, lines 1-6). The primer P1A used in the method has poly A at 5' end (See column 7-8, Table 1). In the quantitative assay, known amounts of in vitro transcribed Q RNA are spiked into the samples prior to RNA extraction, and are thereafter subjected to the same extraction and amplification procedure (See column 5, lines 51-62). The quantitative assay with known amounts of vitro transcribed Q RNA (internal calibrator) is used (See column 11, lines 11-15). The invention of Romano et al. includes a kit for the detection or quantitation of MDC RNA (See column 16, claim 11).

Romano et al. do not disclose a synthetic oligonucleotide which is used to produce a single cRNA species by reverse transcription. However, there is no definition regarding "a synthetic oligonucleotide" in the specification. Moreover, the elements of the synthetic oligonucleotide are the same as a natural nucleic acid sequence. The teaching of Romano et al. read on this limitation.

Romano et al. also do not disclose that the synthetic oligonucleotide comprises an amplicon and a promoter sequence located 3' relative to the amplicon. Nevertheless, Romano et al. disclose that T7 promoter sequence is included in primer P1A (See column 4, lines 24-25 and lines 40-41) located at near to 5' end of the primer (See column 7 and 8, Table 1). As disclosed by Romano et al. the RNA is produced by a transcription based amplification techniques such as

NASBA (See column 7, lines 44-47) in which an oligonucleotide is synthesized by primer P1 comprising a promoter sequence, and then the oligonucleotide is used as a template for producing a double stranded oligonucleotide. The double stranded oligonucleotide comprises an amplicon and a promoter sequence located 3' relative to the amplicon and a RNA is synthesized from a strand of the double stranded oligonucleotide as evidenced by the teachings of Davey et al. (See fig.1 of 5,409,818, issued April. 25, 1995).

Romano et al. do not explicitly disclose the length of the 5' flanking sequence, the 3' flanking sequence, as set forth in claims 23-27. However, the specification discloses that the synthetic oligonuleotide optionally includes a 5' flanking sequence and a 3' flanking sequence. Moreover, there are no metes and bounds recited in the claim regarding the 5' flanking sequence, the 3' flanking sequence and the amplicon. Any sequences in the oligonucleotide synthesized from the method of Romano et al. have a 5' flanking sequence, a 3' flanking sequence and an amplicon. Thus, the teachings of Romano et al. satisfy the limitations of the claims.

Therefore based upon the analysis above, the teachings of Romano anticipate the limitations of the claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 22, 28-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Romano et al. (6,093,542, issued Jul. 25, 2000).

The teachings of Romano et al. are set forth in section 4 above.

Romano et al. do not disclose T7 promoter sequence as recited in SEQ ID NO:1.

Romano et al. disclose a T7 RNA polymerase promoter sequence which comprises SEQ ID NO: 1 as recited in instant claim 4 (See column 4, lines 26-42). SEQ ID NO: 1 of the instant claim is only six nucleotides off from the T7 RNA polymerase promoter sequence of Romano et al.

One of ordinary skill in the art would have been motivated to apply the T7 RNA polymerase promoter sequence of Romano et al. into a calibrator for absolute quantitation of target RNA with a reasonable expectation of success because the primers used in the method of Romano et al. provide a sensitive assay (See column 8, lines 60-67). It would have been prima facie obvious to apply the T7 RNA polymerase promoter sequence of Romano et al. in a calibrator for absolute quantitation of target RNA.

Romano et al. also do not explicitly disclose the length of the amplicon and the synthetic oligonucleotide as recited in claims 28-33.

Romano et al. disclose that the primers P1A and P1B used in the method to produce the oligonucleotides have 49 nucleotides (See column 7 and 8, table 1). It is inherent in the teachings that the amplicon is 30-70 nucleotides in length and the oligonucleotide is 60-140 nucleotideds in length.

One of ordinary skill in the art would have been motivated to apply the amplicon and oligonucleotide of Romano et al. into a calibrator for absolute quantitation of target RNA as claimed because the method of Romano et al. produces the amplicon and oligonucleotide which has the length as claimed. It would have been prima facie obvious to apply the amplicon and the

oligonucleotides with the length as claimed in a calibrator for absolute quantitation of target RNA.

7. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Romano et al. (US 6,093,542, issued July 25, 2000) as applied to claims 19-27, 34-35 and 39-40 above, further in view of Wang et al. (5476774, issued Dec. 19, 1995).

The teachings of Romano et al. are set forth in section 4 above. Romano et al. do not disclose the further limitation of claim 36.

Wang et al. disclose a method of determining the amount of target nucleic acid segment in a sample (See column 3, lines 46-47). Yeast RNA is used in the method (See column 15, lines 1-3).

One of ordinary skill in the art would have been motivated to include a yeast RNA in a calibrator because the method of Wang et al. is preferred for determining the quantity of a special mRNA species and an internal standard is provided useful for quantitation of multiple mRNA species (See the Abstract). It would have been prima facie obvious to include yeast RNA in a calibrator.

8. Claims 38, 41-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Romano et al. (US 6,093,542, issued July 25, 2000) in view of Collins et al. (Analytical Biochemistry, 1995, Vol. 226, pg. 120-129).

The teachings of Romano et al. are set forth in section 4 above.

Regarding claims 45-48 the limitations are addressed in section 4 above

Regarding claim 49-56, the limitations are addressed in section 6 above.

Regarding the limitation "a chemically-synthesized" as recited in claims 42 and 57, there is no definition regarding "a chemically synthesized oligonucleotide" in the specification. Moreover, the elements of the chemically synthesized oligonucleotide are the same as a natural nucleic acid sequence. The teachings of Romano et al. satisfy the limitations of the claims.

Regarding claims 38 and 41, Romano et al. do not disclose measuring cRNA by its absorbance at 260 nm and serial 1:10 dilutions of the cRNA.

Collins et al. disclose that the quantitation is checked by OD_{260} (See pg. 120, the Abstract and pg. 123, column 1, first paragraph) and a method of making RNA standard (See pg. 121-125, Materials and methods). The standard HCV RNAs were serially diluted (See pg. 126, column 1, third paragraph). Collins et al. also indicate that nucleic acid standards can be used to assess the absolute hybridization efficiency of probes, whose specific activity is precisely known, and they can be used to measure the accuracy of quantitation of different probe or primer designs (See pg. 120, column 2).

Collins et al. do not disclose serial 1:10 dilutions.

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply the method of making RNA standard for calibrating the quantitation of RNA because the RNA standard made by Collins et al. is precisely and accurately quantified (See pg. 120, column 2) and reproducible (See pg. 121, column 1, lines 1-2). In addition, one of ordinary skill in the art would have optimized the serial dilutions to 1:10 because it was a routine practice to optimize reaction parameters such as dilution factor. Moreover, one of ordinary skill in the art would have included the serial 1:10 dilution of the cRNA in a kit. It was also a routine practice to include all components in a kit for conveniently performing a method. It would have been prima

facie obvious to apply the method of Collins et al. for generating calibration data for absolute quantitation of RNA or determining nucleic acid molecules.

Summary

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

Joyce Tung
March 5, 2008